

WEST**Freeform Search****Database:**

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 US Pre-Grant Publication Full-Text Database
 JPO Abstracts Database
 EPO Abstracts Database
 Derwent World Patents Index
 IBM Technical Disclosure Bulletins

Term:

((tumor necrosis factor near2 converting enzyme)
 or tace) and hydroxamate

Display:

50

Documents in Display Format:

CIT

Starting with Number

1

Generate: ☐ Hit List ☒ Hit Count ☐ Image

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Search History**Today's Date:** 6/19/2001

<u>DB Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
JPAB,EPAB,DWPI	(adam-17) and hydroxamate	0	<u>L9</u>
JPAB,EPAB,DWPI	((tumor necrosis factor near2 converting enzyme) or tace) and hydroxamate	3	<u>L8</u>
USPT,PGPB	l6 and hydroxamate	2	<u>L7</u>
USPT,PGPB	tumor necrosis factor near2 converting enzyme	12	<u>L6</u>
USPT,PGPB	adam-17 and hydroxamate	0	<u>L5</u>
USPT,PGPB	l3 and @ad<19980812	2	<u>L4</u>
USPT,PGPB	l1 same hydroxamate	5	<u>L3</u>
USPT,PGPB	l1 and hydroxamate	17	<u>L2</u>
USPT,PGPB	tace	61	<u>L1</u>

* * * * *
STN Columbus * * * * *
* * * * *

FILE 'HOME' ENTERED AT
15:34:13 ON 19 JUN 2001

=> file reg
COST IN U.S. DOLLARS
SINCE FILE TOTAL

ENTRY SESSION
FULL ESTIMATED COST
0.15 0.15

FILE 'REGISTRY' ENTERED AT
15:34:47 ON 19 JUN 2001
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STRUCTURE FILE UPDATES: 18
JUN 2001 HIGHEST RN 342370-
76-7
DICTIONARY FILE UPDATES: 18
JUN 2001 HIGHEST RN 342370-
76-7

TSCA INFORMATION NOW CURRENT
THROUGH January 11, 2001

Please note that search-
term pricing does apply when
conducting SmartSELECT
searches.

Structure search limits have
been increased. See HELP
SLIMIT
for details.

=> e tace/cn
E1 1
TACCAOSIDE PERMETHYLATE/CN
E2 1 TACCH/CN
E3 2 --> TACE/CN
E4 1 TACE
(PHARMACEUTICAL)/CN
E5 1 TACE
PROTEINASE/CN
E6 1 TACEF/CN
E7 1 TACFOAM
VCPAC/CN
E8 1
TACHARANITE/CN
E9 1
TACHARANITE
(AL2CA12H6(SIO3)18.15H2O)/CN
E10 1
TACHIGAREN/CN
E11 1
TACHIOGROSIDE B/CN
E12 1
TACHIOSIDE/CN

=> s e3
L1 2 TACE/CN

=> d

L1 ANSWER 1 OF 2 REGISTRY
COPYRIGHT 2001 ACS
RN 151769-16-3 REGISTRY
CN Proteinase, pro-tumor
necrosis factor (9CI) (CA
INDEX NAME)
OTHER NAMES:
CN ADAM17 proteinase
CN Metalloproteinase
ADAM17
CN Pro tumor necrosis
factor cleavage enzyme
CN Pro-tumor necrosis
factor-.alpha.-processing
enzyme
CN ***TACE***
CN TACE proteinase
CN TNF-.alpha. convertase
CN TNF-.alpha. converting
enzyme
CN TNF-.alpha. processing
protease
CN Tumor necrosis factor
.alpha. convertase
CN Tumor necrosis factor-
.alpha. converting enzyme
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS,
BIOTECHNO, CA, CAPLUS, CIN,
EMBASE, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT
AVAILABLE ***

136 REFERENCES
IN FILE CA (1967 TO DATE)
3 REFERENCES
TO NON-SPECIFIC DERIVATIVES
IN FILE CA
137 REFERENCES
IN FILE CAPLUS (1967 TO
DATE)

=> d 2

L1 ANSWER 2 OF 2 REGISTRY
COPYRIGHT 2001 ACS
RN 569-57-3 REGISTRY
CN Benzene, 1,1',1''-(1-
chloro-1-ethenyl-2-
ylidene)tris[4-methoxy-
(9CI) (CA
INDEX NAME)
OTHER CA INDEX NAMES:
CN Chlorotrianisene (6CI)
CN Ethylene, chlorotris(p-
methoxyphenyl)- (7CI, 8CI)
OTHER NAMES:
CN Anisene
CN Chlorotris(p-
methoxyphenyl)ethylene
CN Chlortrianizen
CN Clorestrolo
CN Clorotrisin
CN Hormonisene
CN Khlortrianizen

CN Merbentul
CN Metace
CN NSC 10108
CN Rianil
CN ***Tace***
CN Tace (pharmaceutical)
CN Tri-p-
anisylchloroethylene
CN Trianisylchloroethylene
CN Tris(p-
methoxyphenyl)chloroethylene
FS 3D CONCORD
DR 13003-83-3
MF C23 H21 Cl O3
LC STN Files: ANABSTR,
BEILSTEIN*, BIOBUSINESS,
BIOSIS, BIOTECHNO, CA,
CANCERLIT, CAOLD,
CAPLUS, CBNB, CHEMCATS,
CHEMINFORMRX, CHEMLIST, CIN,
CSCHEM, DDFU,
DIOGENES, DRUGU, EMBASE,
HODOC*, HSDB*, IPA, MEDLINE,
MRCK*, NIOSHTIC,
PROMT, RTECS*, SPECINFO,
TOXLINE, TOXLIT, USAN,
USPATFULL
(*File contains
numerically searchable
property data)
Other Sources:
EINECS**, WHO
(**Enter CHEMLIST
File for up-to-date
regulatory information)

/ Structure 1 in file .gra /
98 REFERENCES
IN FILE CA (1967 TO DATE)
4 REFERENCES
TO NON-SPECIFIC DERIVATIVES
IN FILE CA
98 REFERENCES
IN FILE CAPLUS (1967 TO
DATE)
30 REFERENCES
IN FILE CAOLD (PRIOR TO
1967)

=> set sel cont
SET COMMAND COMPLETED

=> sel l1 1 name
E1 THROUGH E11 ASSIGNED

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT
AUTHORIZED
COST IN U.S. DOLLARS
SINCE FILE TOTAL

ENTRY SESSION
FULL ESTIMATED COST
7.99 8.14

INDEX 'ADISALERTS,
ADISINSIGHT, AGRICOLA,

ANABSTR, AQUASCI,
 BIOBUSINESS,
 BIOCOMMERCE, BIOSIS,
 BIOTECHABS, BIOTECHDS,
 BIOTECHNO, CABA, CANCERLIT,
 CAPLUS, CEABA-VTB,
 CEN, CIN, CONFSCI, CROPB,
 CROPU, DDFB, DDFU, DGENE,
 DRUGB, DRUGLAUNCH,
 DRUGMONOG2, DRUGNL, ...'
 ENTERED AT 15:36:30 ON 19
 JUN 2001

59 FILES IN THE FILE LIST IN
 STNINDEX

Enter SET DETAIL ON to see
 search term postings or to
 view
 search error messages that
 display as 0* with SET
 DETAIL OFF.

=> s el-11
 6 FILE
 ADISALERTS
 10 FILE
 ADISINSIGHT
 2 FILES SEARCHED...
 1 FILE AGRICOLA
 4 FILES SEARCHED...
 1 FILE AQUASCI
 9 FILE
 BIOBUSINESS
 2 FILE
 BIOCOMMERCE
 289 FILE BIOSIS
 8 FILES SEARCHED...
 8 FILE
 BIOTECHABS
 8 FILE BIOTECHDS
 92 FILE BIOTECHNO
 11 FILES SEARCHED...
 7 FILE CABA
 256 FILE CANCERLIT
 13 FILES SEARCHED...
 274 FILE CAPLUS
 14 FILES SEARCHED...
 8 FILE CIN
 12 FILE CONFSCI
 18 FILES SEARCHED...
 1 FILE CROPU
 20 FILES SEARCHED...
 45 FILE DDFB
 63 FILE DDFU
 22 FILES SEARCHED...
 94 FILE DGENE
 45 FILE DRUGB
 24 FILES SEARCHED...
 12 FILE
 DRUGMONOG2
 3 FILE DRUGNL
 70 FILE DRUGU
 28 FILES SEARCHED...
 2 FILE
 DRUGUPDATES
 6 FILE EMBAL
 30 FILES SEARCHED...
 334 FILE EMBASE
 31 FILES SEARCHED...
 124 FILE ESBIODBASE

32 FILES SEARCHED...
 1 FILE FSTA
 100 FILE GENBANK
 37 FILES SEARCHED...
 33 FILE IFIPAT
 56 FILE JICST-
 EPLUS
 40 FILES SEARCHED...
 39 FILE LIFESCI
 43 FILES SEARCHED...
 289 FILE MEDLINE
 2 FILE NIOSHTIC
 45 FILES SEARCHED...
 2 FILE NTIS
 47 FILES SEARCHED...
 104 FILE PASCAL
 48 FILES SEARCHED...
 11 FILE PHAR
 16 FILE PHIN
 96 FILE PROMT
 52 FILES SEARCHED...
 290 FILE SCISEARCH
 54 FILE TOXLINE
 55 FILES SEARCHED...
 52 FILE TOXLIT
 87 FILE USPATFULL
 57 FILES SEARCHED...
 57 FILE WPIDS
 57 FILE WPINDEX

45 FILES HAVE ONE OR MORE
 ANSWERS, 59 FILES SEARCHED
 IN STNINDEX

L2 QUE ("ADAM17
 PROTEINASE"/BI OR
 "METALLOPROTEINASE
 ADAM17"/BI OR "PRO TUMOR
 NECROSIS FACTOR
 CLEAVAGE ENZYME"/BI OR "PRO-
 TUMOR NECROSIS FACTOR-.AL
 PHA.-PROCESSING
 ENZYME"/BI OR "TACE
 PROTEINASE"/BI OR TACE/BI OR
 "TNF-
 .ALPHA.
 CONVERTASE"/BI OR "TNF-
 .ALPHA. CONVERTING
 ENZYME"/BI OR "TNF-
 ALPHA. PROCESSING
 PROTEASE"/BI OR "TUMOR
 NECROSIS FACTOR .ALPHA.
 CONVE
 RTASE"/BI OR "TUMOR
 NECROSIS FACTOR-.ALPHA.
 CONVERTING ENZYME"/BI)

=> s l2 and hydroxamate
 3 FILES SEARCHED...
 12 FILE BIOSIS
 8 FILES SEARCHED...
 9 FILE BIOTECHNO
 11 FILES SEARCHED...
 7 FILE CANCERLIT
 13 FILES SEARCHED...
 24 FILE CAPLUS
 14 FILES SEARCHED...
 18 FILES SEARCHED...
 20 FILES SEARCHED...
 2 FILE DDFU
 22 FILES SEARCHED...

24 FILES SEARCHED...
 2 FILE DRUGU
 28 FILES SEARCHED...
 30 FILES SEARCHED...
 15 FILE EMBASE
 31 FILES SEARCHED...
 11 FILE ESBIODBASE
 32 FILES SEARCHED...
 2 FILE IFIPAT
 39 FILES SEARCHED...
 3 FILE LIFESCI
 42 FILES SEARCHED...
 11 FILE MEDLINE
 44 FILES SEARCHED...
 46 FILES SEARCHED...
 48 FILES SEARCHED...
 1 FILE PROMT
 52 FILES SEARCHED...
 13 FILE SCISEARCH
 3 FILE TOXLINE
 55 FILES SEARCHED...
 1 FILE TOXLIT
 23 FILE USPATFULL
 57 FILES SEARCHED...
 6 FILE WPIDS
 6 FILE WPINDEX

18 FILES HAVE ONE OR MORE
 ANSWERS, 59 FILES SEARCHED
 IN STNINDEX

L3 QUE L2 AND HYDROXAMATE

=> s l3 and py<1999
 0* FILE
 ADISINSIGHT
 3 FILES SEARCHED...
 5 FILES SEARCHED...
 7 FILES SEARCHED...
 6 FILE BIOSIS
 8 FILES SEARCHED...
 5 FILE BIOTECHNO
 11 FILES SEARCHED...
 4 FILE CANCERLIT
 13 FILES SEARCHED...
 12 FILE CAPLUS
 14 FILES SEARCHED...
 17 FILES SEARCHED...
 0* FILE CONFSCI
 19 FILES SEARCHED...
 21 FILES SEARCHED...
 2 FILE DDFU
 23 FILES SEARCHED...
 26 FILES SEARCHED...
 2 FILE DRUGU
 29 FILES SEARCHED...
 5 FILE EMBASE
 31 FILES SEARCHED...
 5 FILE ESBIODBASE
 32 FILES SEARCHED...
 0* FILE FOREGE
 37 FILES SEARCHED...
 2 FILE IFIPAT
 40 FILES SEARCHED...
 1 FILE LIFESCI
 42 FILES SEARCHED...
 0* FILE MEDICONF
 5 FILE MEDLINE
 44 FILES SEARCHED...
 46 FILES SEARCHED...
 48 FILES SEARCHED...

0* FILE PHAR
 52 FILES SEARCHED...
 5 FILE SCISEARCH
 54 FILES SEARCHED...
 1 FILE TOXLINE
 55 FILES SEARCHED...
 6 FILE USPATFULL
 57 FILES SEARCHED...
 1 FILE WPIDS
 58 FILES SEARCHED...
 1 FILE WPINDEX

16 FILES HAVE ONE OR MORE
 ANSWERS, 59 FILES SEARCHED
 IN STNINDEX

L4 QUE L3 AND PY<1999

=> d rank

F1	12	CAPLUS
F2	6	BIOSIS
F3	6	USPATFULL
F4	5	BIOTECHNO
F5	5	EMBASE
F6	5	ESBIOBASE
F7	5	MEDLINE
F8	5	SCISEARCH
F9	4	CANCERLIT
F10	2	DDFU
F11	2	DRUGU
F12	2	IFIPAT
F13	1	LIFESCI
F14	1	TOXLINE
F15	1	WPIDS
F16	1	WPINDEX

=> file f1-2 f4-16
 COST IN U.S. DOLLARS
 SINCE FILE TOTAL

ENTRY	SESSION
FULL ESTIMATED COST	
27.90	36.04

FILE 'CAPLUS' ENTERED AT
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FILE 'BIOSIS' ENTERED AT
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 COPYRIGHT (C) 2001 BIOSIS(R)

FILE 'BIOTECHNO' ENTERED AT
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FILE 'CANCERLIT' ENTERED AT
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FILE 'DDFU' ACCESS NOT
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 CLAIMS(R) Patent Services
 (IFI)

FILE 'LIFESCI' ENTERED AT
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 Scientific Abstracts (CSA)

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FILE 'WPIDS' ENTERED AT
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=> s 14

1	FILES SEARCHED...
2	FILES SEARCHED...
3	FILES SEARCHED...
4	FILES SEARCHED...
5	FILES SEARCHED...
6	FILES SEARCHED...
7	FILES SEARCHED...
8	FILES SEARCHED...
10	FILES SEARCHED...
11	FILES SEARCHED...
12	FILES SEARCHED...

L5 54 L4

=> dup rem 15
 PROCESSING COMPLETED FOR L5
 L6 15 DUP REM L5
 (39 DUPLICATES REMOVED)
 ANSWERS '1-
 12' FROM FILE CAPLUS
 ANSWER '13'
 FROM FILE BIOSIS

ANSWER '14'
 FROM FILE DRUGU

ANSWER '15'
 FROM FILE IFIPAT

=> d bib ab 1-15

L6 ANSWER 1 OF 15 CAPLUS
 COPYRIGHT 2001 ACS
 DUPLICATE 1
 AN 1998:646966 CAPLUS
 DN 130:11872
 TI Phorbol Ester-Induced
 Juxtamembrane Cleavage of
 Angiotensin-Converting
 Enzyme Is Not Inhibited
 by a Stalk Containing
 Intrachain Disulfides
 AU Schwager, Sylva L. U.;
 Chubb, Anthony J.; Scholle,
 Renate R.; Brandt, Wolf
 F.; Eckerskorn,
 Christoph; Sturrock, Edward
 D.; Ehlers, Mario R. W.
 CS Department of Medical
 Biochemistry, University of
 Cape Town Medical
 School, Observatory,
 7925, S. Afr.
 SO Biochemistry (
 1998), 37(44),
 15449-15456

CODEN: BICHAW; ISSN:
 0006-2960
 PB American Chemical
 Society
 DT Journal
 LA English
 AB Specialized proteases,
 referred to as sheddases,
 secretases, or
 membrane-protein-
 solubilizing proteases
 (MPSPs), solubilize the
 extracellular domains
 of diverse membrane proteins
 by catalyzing a
 specific cleavage in
 the juxtamembrane stalk
 regions of such proteins. A
 representative MPSP (
 tumor
 necrosis
 factor -.
 alpha .
 convertase) was
 cloned recently and shown to
 be a
 disintegrin
 metalloprotease that is
 inhibited by peptide
 hydroxamates
 including the compd. TAPI
 (TNF-.alpha. protease
 inhibitor). Substrate
 determinants that specify
 cleavage by MPSPs remain
 incompletely
 characterized, but may
 include the physicochem.
 properties of

the stalk or unidentified recognition motifs in the stalk or the extracellular domain. We constructed a mutant angiotensin-converting enzyme (ACE) in which the stalk has been replaced with an epidermal growth factor (EGF)-like domain (ACE-JMEGF), to test the hypothesis that MPSP cleavage requires an open, comparatively unfolded or extended stalk.

Wild-type ACE is a type I transmembrane (TM) ectoprotein that is efficiently solubilized by a typical MPSP activity. We found that

ACE-JMEGF was solubilized inefficiently and accumulated in a cell-assocd.

form on transfected Chinese hamster ovary (CHO) cells; cleavage was

stimulated by phorbol ester and inhibited by TAPI, features typical of

MPSP activity. Detn. of the C-terminus of sol.

ACE-JMEGF revealed that, surprisingly, cleavage occurred at a Gly-Phe bond between the fifth and

sixth cysteines within the third disulfide loop of the EGF-like domain.

Redn. of intact CHO cells with tributylphosphine resulted in the rapid

release of ACE-JMEGF (but not wild-type ACE) into the medium, suggesting

that a proportion of membrane-bound ACE-JMEGF is cleaved but remains

cell-assocd. via disulfide tethering. The mechanism for the release of

ACE-JMEGF in the absence of chem. redn. is unclear. We conclude that the

presence of a compact, disulfide-bridged domain does not per se inhibit

cleavage by an MPSP activity, but ectodomain release is prevented by disulfide tethering to the TM domain.

RE.CNT 38

RE

(1) Arribas, J; J Biol Chem 1996, V271, P11376 CAPLUS
(2) Arribas, J; J Biol Chem 1997, V272, P17160 CAPLUS

(4) Beldent, V; J Biol Chem 1995, V270, P28962 CAPLUS
(5) Black, R; Nature 1997, V385, P729 CAPLUS
(7) Brakebusch, C; J Biol Chem 1994, V269, P32488 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 15 CAPLUS
COPYRIGHT 2001 ACS

DUPLICATE 2

AN 1998:529532 CAPLUS

TI Succinate-based

tnf -. ***alpha***

. ***convertase***

. inhibitors: 5-

azabenzimidazole as a surrogate of the amide bond at P3'.

AU Xue, Chu-Biao; He, Xiaohua; Roderick, John; DeGrado, William; Jaffee, Bruce; Covington, Maryanne; Magolda, Ron; Decicco, Carl

CS DuPont Merck Pharmaceutical Company, Wilmington, DE, 19880, USA

SO Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27 (***1998***), MEDI-046 Publisher: American Chemical Society, Washington, D. C.

CODEN: 66KYA2

DT Conference; Meeting Abstract

LA English

AB TNF-.alpha. is a key cytokine in inflammation and prodn. of TNF-.alpha. is significantly increased in inflammatory diseases such as rheumatoid arthritis. ***TNF*** -. ***alpha*** . ***convertase*** is responsible for converting the membrane-bound TNF-.alpha. precursor to the

mature sol. TNF-.alpha.. This process has been found to be inhibited by

some succinate-based MMP inhibitors. As part of our efforts in the search for ***TNF*** -. ***alpha*** .

convertase inhibitors, we were interested in succinate-based

hydroxamate compds. with an

amide bond surrogate at P3'. The discovery of 5-azabenzimidazole as a surrogate of the amide bond at P3' will be presented.

L6 ANSWER 3 OF 15 CAPLUS
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DUPLICATE 3

AN 1998:630170 CAPLUS

DN 129:341110

TI ***TNF*** -. ***alpha*** .

converting

enzyme (

TACE) is

inhibited by TIMP-3

AU Amour, Augustin;

Slocombe, Patrick M.;

Webster, Ailsa; Butler, Michael;

Knight, C. Graham; Smith, Bryan J.; Stephens, Paul E.; Shelley, Chris;

Hutton, Mike; Knauper, Vera; Docherty, Andrew J.

P.; Murphy, Gillian

CS School of Biological Sciences, University of

Cambridge, Cambridge, CB2

IQW, UK

SO FEBS Lett. (

1998), 435(1), 39-44

CODEN: FEBLAL; ISSN:

0014-5793

PB Elsevier Science B.V.

DT Journal

LA English

AB Tumor necrosis factor-.alpha. (***TNF*** -. ***alpha*** .)-

converting

enzyme (***TACE***

; ADAM-17) is a

membrane-bound

disintegrin

metalloproteinase that

processes the

membrane-assocd.

cytokine, pro-TNF-.alpha.,

to a sol. form. Because of

its putative

involvement in inflammatory

diseases, ***TACE***

represents a

significant target for the

design of specific synthetic

inhibitors as

therapeutic agents. In

order to study its

inhibition by

TIMPs and synthetic

inhibitors of

metalloproteinases, the

catalytic domain

of mouse ***TACE***

(rTACE) was overexpressed as

a sol. Ig fusion

protein from NS00 cells; rTACE was found to be well inhibited by peptide ***hydroxamate*** inhibitors as well as by TIMP-3, but not by TIMP-1, TIMP-2, or TIMP-4. These results suggest that TIMP-3, unlike the other TIMPs, may be important in the modulation of pathol. events in which TNF-.alpha. secretion is involved.

L6 ANSWER 4 OF 15 CAPLUS
COPYRIGHT 2001 ACS
DUPLICATE 4
AN 1997:70379 CAPLUS
DN 126:171901
TI Preparation of peptide derivatives as inhibitors of TNF-.alpha. secretion
IN Black, Roy A.; Fitzner, Jeffrey N.; Sleath, Paul R.
PA Immunex Corporation, USA
SO U.S., 28 pp. Cont.-in-part of U.S. Ser. No. 110, 601, abandoned.

CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2
PATENT NO. KIND
DATE APPLICATION
NO. DATE

--

PI US 5594106 A
19970114 US 1994-
292547 19940818 <--
US 5629285 A
19970513 US 1996-
651363 19960522 <--
PRAI US 1993-110601
19930823
US 1994-292547
19940818
OS MARPAT 126:171901
AB Peptide derivs. having active groups capable of inhibiting ***TNF*** -.
alpha
converting
enzyme (***TACE***),
such as
hydroxamates ,
thiols, phosphoryls and carboxyls

X(CHR1)mCHR2CONHCHR3CO(A)nNH
BNH2 [I; X = hydroxamic acid, thiol, phosphoryl, carboxyl; m = 0-2; R1, R2, R3 = independently H, alkylene(cycloalkyl), OR4, NR4R5, halo,

(un)substituted C1-8 alkyl, C1-8 alkylenearyl, aryl, (un)protected natural amino acid side chain, R6R7; R4, R5 = independently H, (un)substituted C1-8 alkyl; R6 = (un)substituted C1-8 alkyl; R7 = OR4, NR4R5, halo; n = 0-2; each A = same or different (un)protected .alpha.-amino acid radical; B = (un)substituted C2-8 alkylene), pharmaceutically acceptable salts thereof, and methods for

prepg. them are disclosed. I are useful in inhibiting ***TACE*** responsible for cleavage of TNF-.alpha. precursor to provide biol. active

TNF-.alpha.. Thus, coupling of MeO2CCH2CH(CH2CHMe2)CO2Su (Su = succinimido; prepn. given) with dipeptide H-Nal-Ala-NHCH2CH2NHZ (Nal = 2-naphthyl-L-alanine; Z = CO2CH2Ph; prepn given), condensation with hydroxylamine and catalytic hydrogenolysis, gave ***hydroxamate*** inhibitor II. II shows selective in vitro and in vivo inhibition of TNF-.alpha. secretion.

L6 ANSWER 5 OF 15 CAPLUS
COPYRIGHT 2001 ACS
DUPLICATE 5
AN 1997:332335 CAPLUS
DN 127:132564
TI Partial purification and characterization of a tumor necrosis factor-.alpha. converting activity
AU Robache-Gallea, Sylvie; Bruneau, Jean Michel; Robbe, Hugue; Morand, Valerie; Capdevila, Cecile; Bhatnagar, Neerja; Chouaib, Salem; Roman-Roman, Sergio
CS Domaine Therapeutique Immunologie, Roussel-Uclaf, Romainville, F-93230, Fr.
SO Eur. J. Immunol. (***1997***), 27(5), 1275-1282
CODEN: EJIMAF; ISSN: 0014-2980
PB VCH
DT Journal

LA English
AB Tumor necrosis factor (TNF)-.alpha. is initially synthesized as an extracellular membrane-assocd. 26-kDa protein that is further cleaved at Ala76-Val77 to yield the sol. 17-kDa form. Peptide- ***hydroxamate*** metalloproteinase inhibitors were reported to block the proteolytic processing of TNF-.alpha., thus suggesting that the putative ***TNF*** -. ***alpha*** .
converting
enzyme (***TACE***)

is a Zn-dependent metalloendopeptidase. A TNF-.alpha. converting activity (TACA) was characterized that cleaves in vitro the human 26-kDa TNF-.alpha. at the physiol. processing site. The chromatog. steps followed for purifn. and the use of a panel of proteinase inhibitors indicate that the enzyme responsible for TACA is a membrane glycosylated metalloendopeptidase which is most likely different from the matrix-degrading metalloproteinases. The failure of TACA to process a Val77 .fwdarw. Gly77 precursor mutant emphasizes the importance of hydrophobic residue at P1' position. TACA is not able to cleave the mouse pro-TNF-.alpha. and does not catalyze in vitro the processing of other transmembrane proteins susceptible to metalloproteinase-mediated shedding, such as interleukin-6 or TNF receptors. It was suggested the existence of an enzyme specific for TNF-.alpha. within the metalloproteinases involved in the processing/shedding of a no. of cytokines and cytokine receptors.

L6 ANSWER 6 OF 15 CAPLUS
COPYRIGHT 2001 ACS
DUPLICATE 6
AN 1997:43929 CAPLUS

DN 126:154267
TI Purification of ADAM 10
from bovine spleen as a
TNF

alpha
convertase
AU Lunn, Charles A.; Fan,
Xuedong; Dalie, Barbara;
Miller, Kenneth; Zavodny,
Paul J.; Narula,
Satwant K.; Lundell, Daniel
CS Department of
Immunology, Schering-Plough
Research Institute,
Kenilworth,
NJ, 07033, USA
SO FEBS Lett. (
1997), 400(3), 333-
335

CODEN: FEBLAL; ISSN:
0014-5793
PB Elsevier
DT Journal
LA English
AB The authors have
purified a protease with
characteristics of
TNF

alpha
convertase from
bovine spleen membranes.
Peptide sequencing of
the purified protein
identified it as ADAM 10
(Genbank accession no.
Z21961). This
metalloprotease cleaves a
recombinant
proTNF.alpha. substrate to
mature TNF.alpha., and can
cleave a
synthetic peptide
substrate to yield the
mature TNF.alpha. amino
terminus

in vitro. The enzyme
is sensitive to a
hydroxamate
inhibitor of
MMPs, but insensitive
to phosphoramidon. In
addn., cloned ADAM 10
mediates proTNF.alpha.
processing in a processing-
incompetent cell line.

L6 ANSWER 7 OF 15 CAPLUS
COPYRIGHT 2001 ACS
DUPLICATE 7
AN 1997:64517 CAPLUS
DN 126:156259
TI Further evidence for a
common mechanism for
shedding of cell surface
proteins
AU Muellerberg, Juergen;
Rauch, Charles T.; Wolfson,
Martin F.; Castner,
Beverly; Fitzner,
Jeffrey N.; Otten-Evans,
Carol; Mohler, Kendall M.;

Cosman, David; Black,
Roy A.
CS Immunex Corporation, 51
University Street, Seattle,
WA, 98101, USA
SO FEBS Lett. (
1997), 401(2,3),
235-238

CODEN: FEBLAL; ISSN:
0014-5793
PB Elsevier
DT Journal
LA English
AB Pro-TNF.alpha., Steel
factor, type II IL-1R and
IL-2R.alpha. were
expressed in COS-7
cells and the generation of
their sol. forms was examd.
The release of all four
proteins was strongly
stimulated by the phorbol
ester PMA and
completely blocked by a
hydroxamate -based
inhibitor of
metalloproteases. COS-7
cell membranes were found to
cleave

various synthetic pro-
TNF.alpha. peptides with the
same specificity as a
partially purified
TNF . ***alpha***
converting
enzyme
purified from human
monocytic cells, suggesting
that the
same enzyme may be
responsible for at least
some of the COS-7 cell
shedding activity.

L6 ANSWER 8 OF 15 CAPLUS
COPYRIGHT 2001 ACS
AN 2000:833554 CAPLUS
DN 134:4950
TI Preparation of 1-
phenylsulfonylazine-2-
hydroxamates as
metalloproteinase
inhibitors
IN Zook, Scott E.;
Dagnino, Raymond, Jr.;
Deason, Michael E.; Bender,
Steven

L.; Melnick, Michael J.
PA Agouron
Pharmaceuticals, Inc., USA
SO U.S., 45 pp., Cont.-in-
part of U.S. 5,753,653.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3
PATENT NO. KIND
DATE APPLICATION
NO. DATE

PI US 6153757 A
20001128 US 1998-11971
19980629
WO 9720824 A1
19970612 WO 1996-
US19328 19961205 <--
W: AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, CA,
CH, CN, CU, CZ, DE,
DK, EE, ES, FI,
GB, GE, HU, IL, IS, JP, KE,
KG, KP, KR, KZ, LC,
LK, LR, LS, LT,
LU, LV, MD, MG, MK, MN, MW,
MX, NO, NZ, PL, PT,
RO, RU, SD, SE,
SG, SI, SK, TJ, TM, TR, TT,
UA, UG, US, UZ, VN,
AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD,
SZ, UG, AT, BE, CH, DE, DK,
ES, FI, FR, GB, GR,
IE, IT, LU, MC,
NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, ML,
MR, NE, SN, TD,
TG

US 5753653 A
19980519 US 1996-
759713 19961206 <--
PRAI US 1995-41496 P
19951208
WO 1996-US19328 W
19961205
US 1996-759713 A2
19961206
US 1995-569766 A2
19951208
OS MARPAT 134:4950
AB RZZ1SO2NR1CHR2CONHOH
[I; R = (hetero)aryl; R1R2 =
atoms to complete a
heterocyclic ring; Z =
O or S; Z1 = 1,4-phenylene]
were prepd. Thus,
(R)-N-hydroxy-1-[4-(4-
chlorophenoxy)benzenesulfonyl]-4-(tert-

butoxycarbonyl)piperazine-2-
carboxamide (m.p.
94.6.degree.), prepd. from
(R)-piperazine-2-
carboxylic acid in 4 steps,
demonstrated 77.6%
inhibition
of lung metastases in a
female mouse Lewis lung
carcinoma model at 50
mg/kg (i.p.).
RE.CNT 124
RE
(1) Abdel-Meguid;
Biochemistry 1994, V33(39),
P11671 CAPLUS

(2) Aebischer; Helvetica
Chimica Acta 1989, V72,
P1043 CAPLUS

(3) Amatore; Journal of
Organometallic Chemistry
1990, V390(3), P389 CAPLUS

(4) Anon; EP 276436 1988
CAPLUS

(5) Anon; EP 438223 1991
CAPLUS

ALL CITATIONS AVAILABLE IN
THE RE FORMAT

L6 ANSWER 9 OF 15 CAPLUS
COPYRIGHT 2001 ACS

AN 1998:608610 CAPLUS
DN 129:216923

TI Preparation of peptidyl
reverse ***hydroxamate***
derivatives as
metalloprotease

inhibitors

IN Andrews, Robert Carl;
Andersen, Marc Werner;
Stanford, Jennifer Badiang;
Bubacz, Dulcie Garrido;
Chan, Joseph Howling; Cowan,
David John; Gaul,
Michael David;
McDougald, Darryl Lynn;
Musso, David Lee;
Rabinowitz,

Michael Howard; Wiethé,
Robert William

PA Glaxo Group Ltd., UK
SO PCT Int. Appl., 164 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

PATENT NO. KIND
DATE APPLICATION
NO. DATE

PI WO 9838179 A1
19980903 WO 1998-
EP1015 19980224 <--

W: AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, CA,
CH, CN, CU, CZ, DE,

DK, EE, ES, FI,
GB, GE, GH, GM, GW, HU, ID,
IL, IS, JP, KE, KG,

KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MX,

NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK,
SL, TJ, TM, TR, TT,

UA, UG, US, UZ,
VN, YU, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS,
MW, SD, SZ, UG, ZW, AT, BE,
CH, DE, DK, ES, FI,

FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, BF,
BJ, CF, CG, CI, CM,

GA, GN, ML, MR,
NE, SN, TD, TG

AU 9868223 A1
19980918 AU 1998-68223

19980224 <--
BR 9807763 A

20000222 BR 1998-7763
19980224

EP 1019386 A1
20000719 EP 1998-
913575 19980224

R: AT, BE, CH, DE,
DK, ES, FR, GB, GR, IT, LI,
LU, NL, SE, MC, PT,
IE, SI, LT, LV,

FI, RO
NO 9904103 A

19991025 NO 1999-4103
19990825

PRAI US 1997-39112 P
19970226

WO 1998-EP1015 W
19980224

OS MARPAT 129:216923
AB A family of matrix
metalloproteinase (MMP)

inhibitors having general
structural formula I [W
= reverse hydroxamic acid
group N(OH)CHO; R1 =

noteq. H; R4 =
lipophilic substituent; R5 =

H, alkyl; R6 = heteroaryl;
preferably, R1 = Me,

Et, CHMe2, Pr, CH2CH2CF3; R2
= CH2CHMe2, CHMeEt; R3 =

H; R4 = CMe3, CHMeEt,
CHMeOMe, 2-(2-
pyridylcarbonylamino)ethyl;

R5 = H; R6
= 2-thiazolyl, 2-
pyridyl] is described. Such
compsd. show potent

inhibition of MMP's,
cell-free tumor necrosis
factor (TNF) convertase

enzyme and TNF release
from cells, and in some
cases inhibit TNF

convertase and TNF
release from cells in
preference to matrix

metalloproteases.
Thus, reverse

hydroxamate peptide
II, prepd.

in 11 steps from Me
(3R)-hydroxypentanoate,
methallyl bromide,

O-
(tetrahydropyranyl)hydroxyla
mine, Boc-Lys(Cbz)-OH, and
2-aminothiazole,

inhibited ***TNF***
alpha

converting
enzyme

collagenase-1, collagenase-
3, gelatinase B, and

stromelysin 1 all with
Ki <100 nm. II also
inhibited TNF.alpha. release
with IC50 <100 nM.

L6 ANSWER 10 OF 15 CAPLUS
COPYRIGHT 2001 ACS

AN 1997:655428 CAPLUS
DN 127:304777

TI Mammalian ***tumor***
necrosis
factor

alpha
convertase

recombinant expression and
purification, and

screening for hydroxamic
acid deriv. or other

inhibitors
useful for disease

treatment
IN McGeehan, Gerard M.;

Becherer, James David; Moss,
Marcia L.; Schoenen,

Frank J.; Rocque,
Warren J.; Chen, Wen-Ji;

Didsbury, John R.; Jin,
Shiow-Lian Catherine

PA Glaxo Group Limited,
UK; McGeehan, Gerard M.;

Becherer, James David; Moss,
Marcia L.; Schoenen,

Frank J.; Rocque, Warren J.;

Chen, Wen-Ji; Didsbury,
John R.; Jin, Shiow-

Lian Catherine
SO PCT Int. Appl., 132 pp.

CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

PATENT NO. KIND
DATE APPLICATION
NO. DATE

PI WO 9735538 A2
19971002 WO 1997-

EP1497 19970325 <--
WO 9735538 A3

19971120
W: AL, AM, AT, AU,

AZ, BA, BB, BG, BR, BY, CA,
CH, CN, CU, CZ, DE,

DK, EE, ES, FI,
GB, GE, GH, HU, IL, IS, JP,

KE, KG, KP, KR, KZ,
LC, LK, LR, LS,

LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL,

PT, RO, RU, SD,
SE, SG, SI, SK, TJ, TM, TR,

TT, UA, UG, US, UZ,
VN, YU, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW,

SD, SZ, UG, AT, BE, CH, DE,
DK, ES, FI, FR, GB,

GR, IE, IT, LU,
MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN,
ML, MR, NE, SN,
TD, TG

CA 2249985 AA
19971002 CA 1997-
2249985 19970325 <--
AU 9722913 A1
19971017 AU 1997-22913
19970325 <--

EP 900272 A2
19990310 EP 1997-
915426 19970325
R: AT, BE, CH, DE,
DK, ES, FR, GB, GR, IT, LI,
LU, NL, SE, MC, PT,

IE, FI
JP 2000507943 T2
20000627 JP 1997-
534033 19970325
PRAI US 1996-620663 A
19960326

WO 1997-EP1497 W
19970325
AB The present invention
relates to tumor necrosis
factor .alpha.
(TNF.alpha.), and more
specifically to the enzyme
TNF

alpha .-
convertase
(TNF.alpha.-con) that can
proteolytically convert
TNF.alpha. precursor to
mature TNF.alpha.. The
present invention
provides DNA sequences
encoding mammalian
TNF.alpha.-con
and functional equiv.
thereof, recombinant
expression vectors
comprising
said DNA sequences,
host cell lines comprising
said expression vectors,
inhibitors of
TNF.alpha.-con, inhibitors
modified for use as ligands
for

affinity purifn. of
TNF.alpha.-con, and methods
for treating diseases or
conditions resulting
from abnormal levels of
TNF.alpha. in a mammalian
subject. The general
invention is exemplified by
prepn. of a biotinylated
inhibitor of
TNF.alpha.-con.

L6 ANSWER 11 OF 15 CAPLUS
COPYRIGHT 2001 ACS
AN 1997:489857 CAPLUS
TI The inhibition of
metalloproteinases by
macrocyclic sulfonamide
hydroxamates

AU Cherney, Robert J.;
Meyer, Dayton T.; Wang, Li;
Xue, Chu-Baio; Copeland,
Robert A.; Arner,
Elizabeth C.; Jaffee, Bruce
D.; Covington, Maryanne B.;
Decicco, Carl P.
CS Experimental Station,
DuPont Merck Pharmaceutical
Co., Wilmington, DE,
19880-0500, USA

SO Book of Abstracts,
214th ACS National Meeting,
Las Vegas, NV, September
7-11 (***1997***),
MEDI-099 Publisher: American
Chemical Society,
Washington, D. C.
CODEN: 64RNAO

DT Conference; Meeting
Abstract
LA English
AB Metalloproteinases are
involved in the breakdown of
connective tissues and
cartilage as assocd.
with rheumatoid and
osteoarthritis. As a
result, we
became interested in
the inhibition of several
zinc-dependent
endopeptidases
including matrix
metalloproteinases (MMPs)
and the
TNF-converting enzyme,
TACE. In order to
gain metabolic
stability and increase
potency for our inhibitors,
we synthesized a series
of macrocyclic
hydroxamates. The
macrocycles are linked from
P1

to P2' through a
sulfonamide and are
represented by the general
formula 1.

L6 ANSWER 12 OF 15 CAPLUS
COPYRIGHT 2001 ACS
AN 1997:489854 CAPLUS
TI Novel cyclophane
inhibitors of matrix
metalloproteinases and
TNF

-. ***alpha***
converting
enzyme
AU Decicco, Carl P.;
Nelson, David J.; Xue, C. -
B.; Hardman, Karl; Copeland,
Robert; Covington,
Maryanne; Magolda, Ron;
Arner, Elizabeth
CS Chemical and Physical
Science and Inflammatory
Diseases Research, Dupont

Merck Pharmaceutical
Company, Wilmington, DE,
19880-0500, USA
SO Book of Abstracts,
214th ACS National Meeting,
Las Vegas, NV, September
7-11 (***1997***),
MEDI-096 Publisher: American
Chemical Society,
Washington, D. C.
CODEN: 64RNAO
DT Conference; Meeting
Abstract
LA English
AB A novel series of 14,15
and 16-membered ring
cyclophane

hydroxamates
was designed based on the
extended conformation of
the corresponding
peptide based succinate
hydroxamic acid inhibitors
of

metalloproteinases.
The key step in the
synthesis features a high
yielding cyclization of
a p-hydroxy Ph group in P2'
to a 3-carbon bromide
installed in P1. The
resulting compds. were detd.
to be potent inhibitors
of MMPs and
TACE. The prototype
14 membered ring cyclophane
was

crystd. in the active
site of MMP-3 confirming the
extended binding
conformation of the
inhibitor. The synthesis,
in vitro and in vivo
profile of these
inhibitors will be
presented.

L6 ANSWER 13 OF 15 BIOSIS
COPYRIGHT 2001 BIOSIS
AN 1997:428711 BIOSIS
DN PREV199799727914

TI The inhibition of
metalloproteinases by
macrocyclic sulfonamide
hydroxamates

AU Cherney, Robert J.;
Meyer, Dayton T.; Wang, Li;
Xue, Chu-Baio; Copeland,
Robert A.; Arner,
Elizabeth C.; Jaffee, Bruce
D.; Covington, Maryanne B.;
Decicco, Carl P.
CS The DuPont Merck
Pharmaceutical Co., Chemical
and Physical Sci. and
Inflammatory Diseases
Res., Experimental Stn.,
Wilmington, DE 19880-0500
USA

SO Abstracts of Papers
American Chemical Society,
(1997) Vol. 214, No. 1-2,
pp. MEDI 99.
Meeting Info.: 214th
American Chemical Society
National Meeting Las Vegas,
Nevada, USA September
7-11, 1997
ISSN: 0065-7727.
DT Conference; Abstract
LA English

L6 ANSWER 14 OF 15 DRUGU
COPYRIGHT 2001 DERWENT
INFORMATION LTD
AN 1997-43876 DRUGU C
B P
TI Novel cyclophane
inhibitors of matrix
metalloproteinases and
TNF

- ***alpha***
converting
enzyme
AU Decicco C P; Nelson D
J; Xue C B; Hardman K;
Copeland R; Covington M;
Arner E
CS DuPont-Merck
LO Wilmington, Del., USA
SO Abstr.Pap.Am.Chem.Soc.
(214 Meet., Pt. 1, MEDI 096,
1997)

CODEN: ACSRAL
ISSN: 0065-7727
AV Chemical and Physical
Science and Inflammatory
Diseases Research, The
DuPont Merck
Pharmaceutical Company,
Wilmington, DE, 19880-0500.
U.S.A.

LA English
DT Journal
FA AB; LA; CT
FS Literature
AB A novel series of 14,
15 and 16-membered ring
cyclophane

hydroxamates
was designed based on the
extended confirmation of
the corresponding
peptide-based succinate
hydroxamic acid inhibitors
of

metalloproteinases.
The key step in the
synthesis involved a high
yielding cyclization
of a p-hydroxy phenyl group
in P2' to a 3-carbon

bromide installed in
P1. The resulting compounds
were potent inhibitors
of MMPs and

TACE. The prototype
14-membered ring cyclophane

was crystallized in
the active site of MMP-3
confirming the extended
binding conformation
of the inhibitor. The
synthesis, in-vitro and
in-vivo profile of
these inhibitors, such as
SE-205, were presented.
(conference abstract).

L6 ANSWER 15 OF 15 IFIPAT
COPYRIGHT 2001 IFI
AN 2840886
IFIPAT;IFIUDB;IFICDB
TI INHIBITORS OF TNF-
ALPHA SECRETION; AMINO ACID
DERIVATIVES
INF Black, Roy A, Seattle,
WA

Fitzner, Jeffrey N,
Seattle, WA
Sleath, Paul R,
Seattle, WA
IN Black Roy A; Fitzner
Jeffrey N; Sleath Paul R
PAF Immunex Corporation,
Seattle, WA

PA Immunex Corp (9809)
EXNAM Conrad, Joseph
AG Malaska, Stephen L
PI US 5629285

19970513 (CITED IN 003
LATER PATENTS)
AI US 1996-651363
19960522

XPD 23 Aug 2013
RLI US 1993-110601
19930823 CONTINUATION-IN-
PART ABANDONED

US 1994-292547
19940818 DIVISION
FI US 5629285
19970513

DT UTILITY
FS CHEMICAL
CLMN 19
AB Compounds and methods
are disclosed that are
useful in inhibiting the

TNF -

Alpha
converting
enzyme (

TACE)
responsible for cleavage of
TNF- Alpha precursor to
provide biologically
active TNF- Alpha. The
compounds employed in the
invention are peptidyl
derivatives having active
groups capable of

inhibiting
TACE such as,
hydroxamates ,
thiols,
phosphoryls and
carboxyls.

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FULL ESTIMATED COST
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DISCOUNT AMOUNTS (FOR
QUALIFYING ACCOUNTS)
SINCE FILE TOTAL

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CA SUBSCRIBER PRICE
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CA INDEXING COPYRIGHT (C)
2001 AMERICAN CHEMICAL
SOCIETY (ACS)

FILE COVERS 1971 TO PATENT
PUBLICATION DATE: 19 Jun
2001 (20010619/PD)
FILE LAST UPDATED: 19 Jun
2001 (20010619/ED)
HIGHEST PATENT NUMBER:
US6249914
CA INDEXING IS CURRENT
THROUGH 19 Jun 2001
(20010619/UPCA)
ISSUE CLASS FIELDS (/INCL)
CURRENT THROUGH: 19 Jun 2001
(20010619/PD)
REVISED CLASS FIELDS (/NCL)
LAST RELOADED: Apr 2001
USPTO MANUAL OF
CLASSIFICATIONS THESAURUS
ISSUE DATE: Apr 2001

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end of the day. <<<
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field are available the
following week. <<<

>>> Complete CA file
indexing for chemical
patents (or equivalents) <<<
>>> is included in file
records. A thesaurus is
available for the <<<
>>> USPTO Manual of
Classifications in the /NCL,
/INCL, and /RPCL <<<
>>> fields. This thesaurus
includes catchword terms
from the <<<
>>> USPTO/MOC subject
headings and subheadings.
Thesauri are also <<<

>>> available for the WIPO
International Patent
Classification <<<
>>> (IPC) Manuals, editions
1-6, in the /IC1, /IC2,
/IC3, /IC4, <<<
>>> /IC5, and /IC (/IC6)
fields, respectively. The
thesauri in <<<
>>> the /IC5 and /IC fields
include the corresponding
catchword <<<
>>> terms from the IPC
subject headings and
subheadings. <<<

This file contains CAS
Registry Numbers for easy
and accurate
substance identification.

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=> s 14
      1 "ADAM17"/BI
      6336
"PROTEINASE"/BI
      1356
"PROTEINASES"/BI
      6935
"PROTEINASE"/BI
(("PROTEINASE" OR
"PROTEINASES")/BI)
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(("ADAM17"(W)"PROTEINASE")/B
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"METALLOPROTEINASES")/BI)
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      34268 "PRO"/BI
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      21039 "TUMORS"/BI
      36424 "TUMOR"/BI
      ("TUMOR"
OR "TUMORS")/BI)
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"NECROSISES"/BI
      12582 "NECROSIS"/BI
(("NECROSIS" OR
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      61736 "ENZYMES"/BI
      91672 "ENZYME"/BI
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OR "ENZYMES")/BI)
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NECROSIS FACTOR CLEAVAGE
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      428 "PROS"/BI
      34268 "PRO"/BI
      ("PRO" OR
"PROS")/BI)
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      21039 "TUMORS"/BI
      36424 "TUMOR"/BI
      ("TUMOR"
OR "TUMORS")/BI)
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OR "FACTORS")/BI)
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      320794 "ALPHA"/BI
      ("ALPHA"
OR "ALPHAS")/BI)
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"PROCESSINGS"/BI
      628354
"PROCESSING"/BI
      ("PROCESSING" OR
"PROCESSINGS")/BI)
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      61736 "ENZYMES"/BI
      91672 "ENZYME"/BI
      ("ENZYME"
OR "ENZYMES")/BI)
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NECROSIS FACTOR-ALPHA.-
PROCESSING ENZYME"/BI
      ("PRO"(W)"TUMOR"(W)"NECROSI
```

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S"(W)"FACTOR"(W)"ALPHA"(W)"P
ROCESS
      ING"(W)"ENZYME")/BI)
      60 "TACE"/BI
      2 "TACES"/BI
      62 "TACE"/BI,
      ("TACE" OR
"TACES")/BI)
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"PROTEINASE"/BI
      ("PROTEINASE" OR
"PROTEINASES")/BI)
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PROTEINASE"/BI
      ("TACE"(W)"PROTEINASE")/BI)
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      2 TACES/BI
      62 TACE/BI
      ("TACE OR
TACES)/BI)
      5574 "TNF"/BI
      99 "TNFS"/BI
      5588 "TNF"/BI
      ("TNF" OR
"TNFS")/BI)
      320774 "ALPHA"/BI
      256 "ALPHAS"/BI
      320794 "ALPHA"/BI
      ("ALPHA"
OR "ALPHAS")/BI)
      266
"CONVERTASE"/BI
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"CONVERTASES"/BI
      301
"CONVERTASE"/BI
      ("CONVERTASE" OR
"CONVERTASES")/BI)
      20 "TNF-.ALPHA.
CONVERTASE"/BI
      ("TNF"(W)"ALPHA"(W)"CONVERT
ASE")/BI)
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      99 "TNFS"/BI
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      ("TNF" OR
"TNFS")/BI)
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      256 "ALPHAS"/BI
      320794 "ALPHA"/BI
      ("ALPHA"
OR "ALPHAS")/BI)
      225587
"CONVERTING"/BI
      6
"CONVERTINGS"/BI
      225587
"CONVERTING"/BI
      ("CONVERTING" OR
"CONVERTINGS")/BI)
      74834 "ENZYME"/BI
```

61736 "ENZYMES"/BI
 91672 "ENZYME"/BI
 ("ENZYME"
 OR "ENZYMES")/BI)
 36 "TNF-.ALPHA.
 CONVERTING ENZYME"/BI
 ("TNF" (W) "ALPHA" (W) "CONVERT
 ING" (W) "ENZYME")/BI)
 5574 "TNF"/BI
 99 "TNFS"/BI
 5588 "TNF"/BI
 ("TNF" OR
 "TNFS")/BI)
 320774 "ALPHA"/BI
 256 "ALPHAS"/BI
 320794 "ALPHA"/BI
 ("ALPHA"
 OR "ALPHAS")/BI)
 627666
 "PROCESSING"/BI
 9597
 "PROCESSINGS"/BI
 628354
 "PROCESSING"/BI
 ("PROCESSING" OR
 "PROCESSINGS")/BI)
 18013 "PROTEASE"/BI
 11194
 "PROTEASES"/BI
 22142 "PROTEASE"/BI
 ("PROTEASE" OR
 "PROTEASES")/BI)
 0 "TNF-.ALPHA.
 PROCESSING PROTEASE"/BI
 ("TNF" (W) "ALPHA" (W) "PROCESS
 ING" (W) "PROTEASE")/BI)
 30736 "TUMOR"/BI
 21039 "TUMORS"/BI
 36424 "TUMOR"/BI
 ("TUMOR"
 OR "TUMORS")/BI)
 12581 "NECROSIS"/BI
 1
 "NECROSISES"/BI
 12582 "NECROSIS"/BI
 ("NECROSIS" OR
 "NECROSISES")/BI)
 321994 "FACTOR"/BI
 293260 "FACTORS"/BI
 503455 "FACTOR"/BI
 ("FACTOR"
 OR "FACTORS")/BI)
 320774 "ALPHA"/BI
 256 "ALPHAS"/BI
 320794 "ALPHA"/BI
 ("ALPHA"
 OR "ALPHAS")/BI)
 266
 "CONVERTASE"/BI
 124
 "CONVERTASES"/BI
 301
 "CONVERTASE"/BI
 ("CONVERTASE" OR
 "CONVERTASES")/BI)

3 "TUMOR
 NECROSIS FACTOR .ALPHA.
 CONVERTASE"/BI
 ("TUMOR" (W) "NECROSIS" (W) "FA
 CTOR" (W) "ALPHA" (W) "CONVERTAS
 E")/BI
)
 30736 "TUMOR"/BI
 21039 "TUMORS"/BI
 36424 "TUMOR"/BI
 ("TUMOR"
 OR "TUMORS")/BI)
 12581 "NECROSIS"/BI
 1
 "NECROSISES"/BI
 12582 "NECROSIS"/BI
 ("NECROSIS" OR
 "NECROSISES")/BI)
 321994 "FACTOR"/BI
 293260 "FACTORS"/BI
 503455 "FACTOR"/BI
 ("FACTOR"
 OR "FACTORS")/BI)
 320774 "ALPHA"/BI
 256 "ALPHAS"/BI
 320794 "ALPHA"/BI
 ("ALPHA"
 OR "ALPHAS")/BI)
 225587
 "CONVERTING"/BI
 6
 "CONVERTINGS"/BI
 225587
 "CONVERTING"/BI
 ("CONVERTING" OR
 "CONVERTINGS")/BI)
 74834 "ENZYME"/BI
 61736 "ENZYMES"/BI
 91672 "ENZYME"/BI
 ("ENZYME"
 OR "ENZYMES")/BI)
 17 "TUMOR
 NECROSIS FACTOR-.ALPHA.
 CONVERTING ENZYME"/BI
 ("TUMOR" (W) "NECROSIS" (W) "FA
 CTOR" (W) "ALPHA" (W) "CONVERTIN
 G" (W) "
 ENZYME")/BI)
 632 HYDROXAMATE
 291 HYDROXAMATES
 784 HYDROXAMATE
 (HYDROXAMATE OR
 HYDROXAMATES)
 2425056 PY<1999
 L7 6 L3 AND
 PY<1999
 => d ti 1-6
 L7 ANSWER 1 OF 6
 USPATEFULL
 TI Metalloproteinase
 inhibitors and intermediates
 useful for their
 preparation

L7 ANSWER 2 OF 6
 USPATEFULL
 TI Thioaryl sulfonamide
 hydroxamic acid compounds
 L7 ANSWER 3 OF 6
 USPATEFULL
 TI Mammalian ***TNF***
 -. ***alpha***
 convertases
 L7 ANSWER 4 OF 6
 USPATEFULL
 TI Metalloproteinase
 inhibitors, pharmaceutical
 compositions containing
 them and their
 pharmaceutical uses
 L7 ANSWER 5 OF 6
 USPATEFULL
 TI Inhibitors of TNF-
 .alpha. secretion
 L7 ANSWER 6 OF 6
 USPATEFULL
 TI Inhibitors of TNF-
 .alpha. secretion
 => d pn 1-6
 L7 ANSWER 1 OF 6
 USPATEFULL
 PI US 6153757 20001128
 WO 9720824 19970612
 <--
 L7 ANSWER 2 OF 6
 USPATEFULL
 PI US 6087359 20000711
 WO 9839313 19980911
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 L7 ANSWER 3 OF 6
 USPATEFULL
 PI US 5853977 19981229
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 L7 ANSWER 4 OF 6
 USPATEFULL
 PI US 5753653 19980519
 <--
 L7 ANSWER 5 OF 6
 USPATEFULL
 PI US 5629285 19970513
 <--
 L7 ANSWER 6 OF 6
 USPATEFULL
 PI US 5594106 19970114
 <--
 => log y
 COST IN U.S. DOLLARS
 SINCE FILE TOTAL
 ENTRY SESSION

FULL ESTIMATED COST
6.94 177.63

DISCOUNT AMOUNTS (FOR
QUALIFYING ACCOUNTS)
SINCE FILE TOTAL

ENTRY SESSION
CA SUBSCRIBER PRICE
0.00 -7.06

STN INTERNATIONAL LOGOFF AT
16:27:34 ON 19 JUN 2001